

History, Scandals and Tragedies: Beecher, Tuskegee, Willowbrook and the Rest

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University of Wisconsin School of Medicine and Public Health

September 26, 2012

U.S. legislation as response to tragedy

The Patent Medicine Evil



COCAINE
TOOTHACHE DROPS
Instantaneous Cure!
PRICE 15 CENTS.
Prepared by the
LLOYD MANUFACTURING CO.
219 HUDSON AVE., ALBANY, N. Y.
For sale by all Druggists.
(Registered March 1885.) See other side.



Collier's
THE NATIONAL WEEKLY

THE
MOST VULNERABLE POINT
AVAILABLE TO THE PUBLIC
FOR THE YEAR.

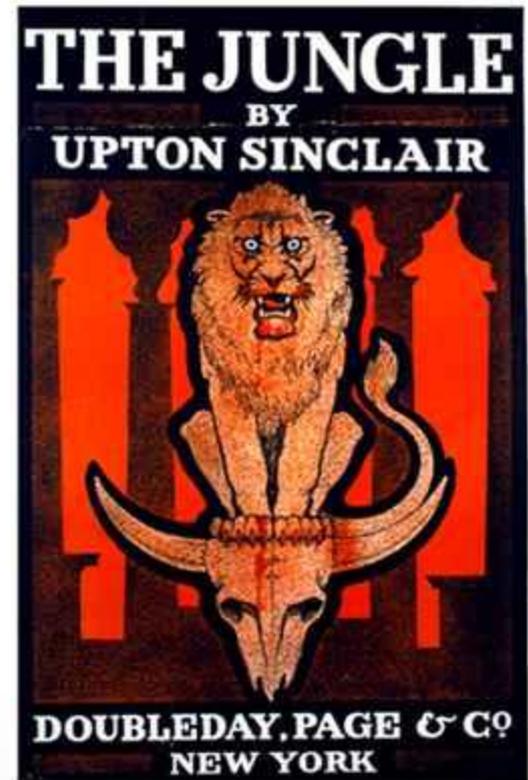
DRUGS LABORATORY

ANOTHER OF COLLIER'S CRUISING CARTOONS OF 1906

Safety of the food supply



Food and Drug Act 1906



Diet dangers c. 1930s

Elixir of Sulfanilamide tragedy

107 deaths

AT YOUR END OF THE COAL CHEMICAL PIPELINE . . .



NEW
Magic Bullets
for
Murdering Microbes

Coal chemicals are the steadfast allies of the medical scientist in his uphill conquest of disease. Pyridine, for example, is vital in the manufacture of sulfa drugs. And gamma-picoline, another valuable Pittsburgh coal chemical, is the source of isonicotinic acid hydrazide, the drug which has shown bright promise in the experimental treatment of tuberculosis in recent months.

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WEEK 1943

Alkyl methyl pyridinium chloride
Benzene meta, para-Cresol ortho-Cresol
Naphthalene Phenol Phthalic Anhydride
alpha-Picoline beta, gamma-Picoline
Isonicotinic Acid
Pyridine Sodium Cyanide
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Click the "X" in the upper right hand corner of this window to return

ONE GALLON ELIXIR ONE GALLON

SULFANILAMIDE

Each fluidounce represents:
Sulfanilamide, 40 grs.

**SUGGESTED FOR THE TREATMENT OF ALL CONDITIONS
IN WHICH THE HEMOLYTIC STREPTOCOCCI APPEAR**

Dose, begin with 2 to 3 teaspoonfuls in water every four hours. Decrease in twenty-four to forty-eight hours to 1 or 2 teaspoonfuls and continue at this dose until recovery.



THE S. E. MASSENGILL COMPANY
Manufacturing Pharmacists
BRISTOL, TENN.-VA.

Please do not copy or reproduce this picture in any way.

Food, Drug and Cosmetic Act of 1938

- Drugs or cosmetics must be tested for toxicity before marketing.
- Adequate directions for use needed to be on package
- Some drugs are designated “by prescription only”

Cranberry crisis of 1959

- Concerns about safety of pesticides used on Cranberries

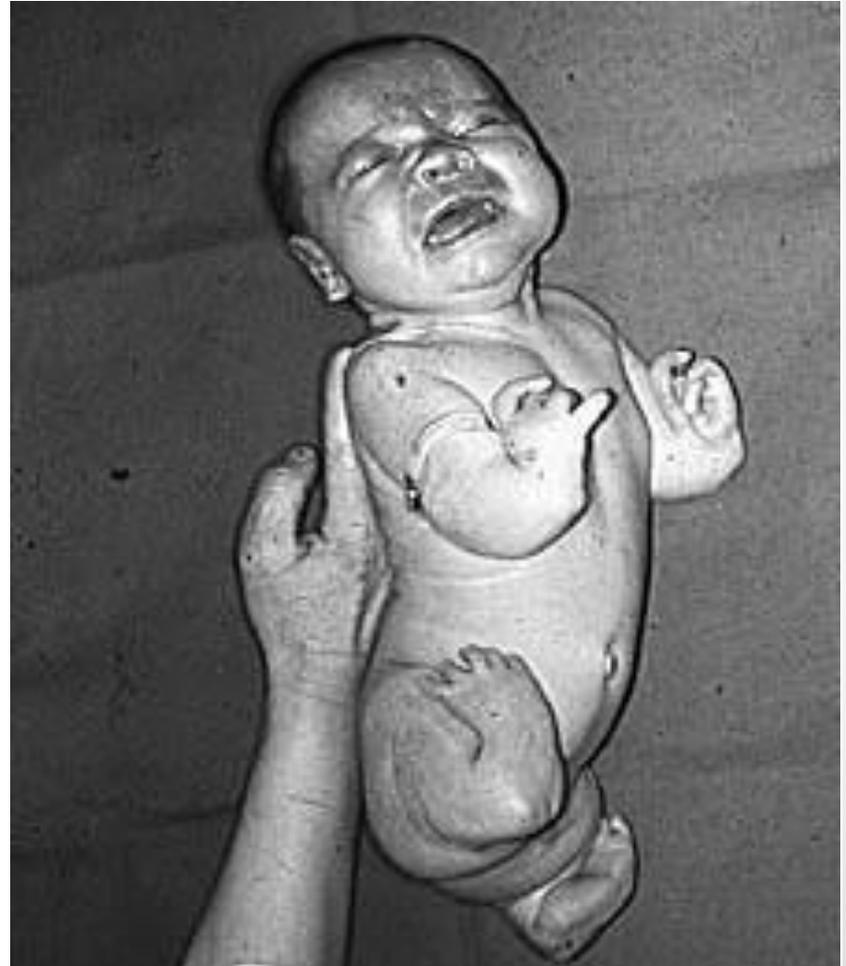


Thalidomide

1960-1961

83 children were born with unusual birth defects, not linked to thalidomide use.

a German scientist makes connections between thalidomide use and thousands of babies born with birth defects.



Kefauver-Harris Amendments to FDA

Frances Kelsey, FDA



FDA can
demand
scientific data
to determine
the drug
works

Congress passes
Animal Welfare Act,
1966

Life magazine 1966

LIFE
Vol. 61, No. 3 Feb. 6, 1966

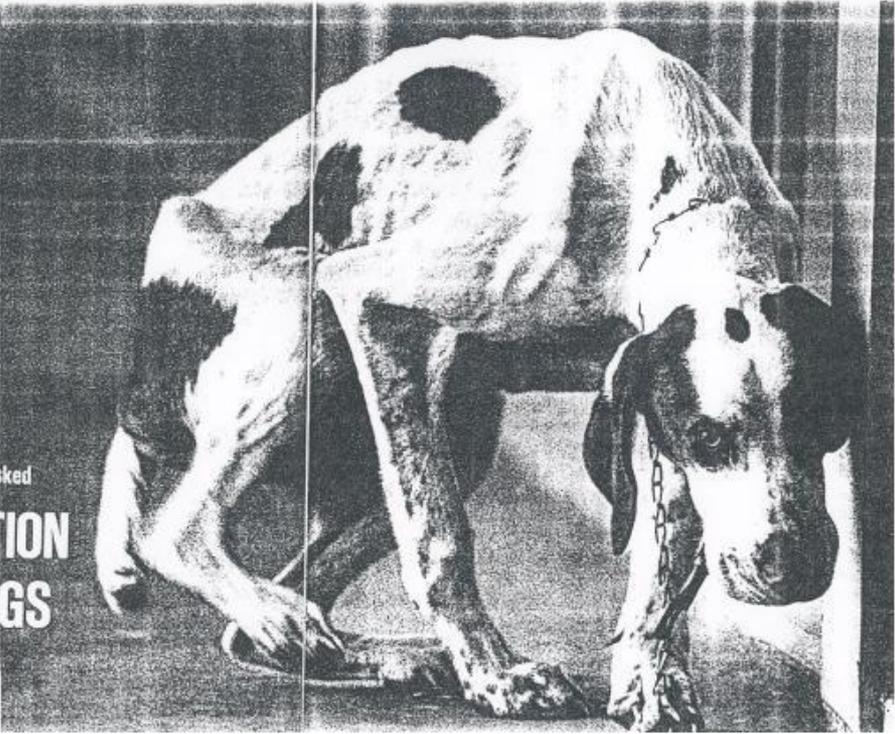
The dog's name is Lucky. He is a seven-colored English pointer with a fine head and good size of good, expressive boning. But when a search from the Animal Protection League came across Lucky at a dog show in St. Louis, Ohio, last month, his name was not on the list—a pointer, associated with hunting, covering, bounding and so forth. The woman bought him for \$1 plus a dollar for the club.

Lucky has his counterparts all over the U.S. Unscrupulous dog "dealers," taking advantage of the growing demand for dogs for vital medical research, are running a lucrative pet recovery business. Laboratories now need almost two million dogs a year. In order to do this, they kidnap dogs from the country, paying a head or two to anyone who comes forward with a dog, and no questions asked. Puppies are, trained to obedience and easy to handle, are usually priced, and the thousands of dogs in the U.S. are estimated that 50 percent of all missing pets have been stolen by "dealers," who in turn sell them to the dealer.

Some dealers keep big inventories of dogs in warehouses, others compound the same source, and regarding their the concentration camps of World War II. Many do not sell directly to the lab, but simply dispose of their pets in private where the program is still a secret, program, when attached to their own work, all for the same, stated by reference to a Human Rehabilitation of such programs are provided by the continuing care of these camps by funding activities. Can you slowly his right, the program, which would contain these shameful conditions.

Pets for sale cheap—no questions asked

CONCENTRATION CAMPS FOR DOGS



Why do we have
federal regulations for
human
experimentation?

In response to scandals and
tragedies Congress passes the
National Research Act

1974

Both the history of human experimentation and history of controversy over human experimentation much older

United States Congress, 1900

considers Senate bill 3424:

a law that would require investigators to disclose in advance the purpose and procedures of any non-therapeutic experiment involving human beings.



Senate bill 3424

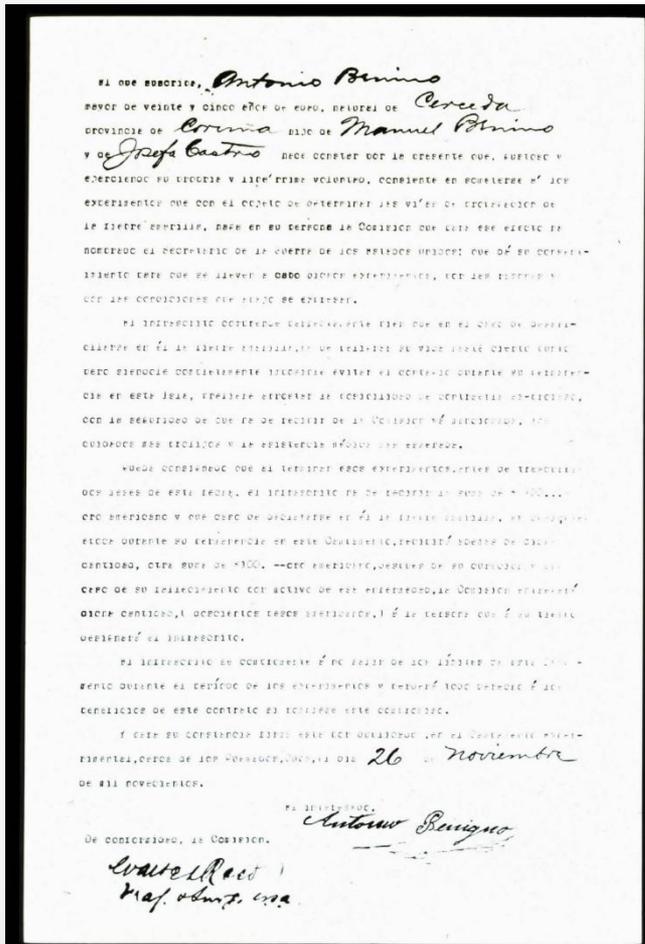
calls for explicit ban on experiments
using those persons deemed unable
to consent,
including
infants,
children under the age of twenty-
one,
and pregnant women.

The Yellow Fever Board in Cuba, 1900



Reed and his colleagues introduce written permission forms

available in both
English and Spanish



The undersigned understands...

perfectly well that in case of the development of yellow fever in him, that he endangers his life to a certain extent but it being entirely impossible for him to avoid the infection during his stay in this island, he prefers to take the chance of contracting it intentionally in the belief that he will receive from the said Commission the greatest care and the most skillful medical service.

Subjects receive \$100 in gold,
\$200 if death occurs



“A written consent was obtained from each one, so that our moral responsibility was to a certain extent lessened. Of course, only the healthiest specimens were experimented upon . . .”

Aristides Agramonte

•

•

Medical research in US

continuing social support for American researchers

celebrating the heroes and martyrs of medical research

self-experimentation and volunteers



3/25/52

NVT

TI

Contaminated Blood Injection Kills Youth In Seattle Preservation Research Project

SEATTLE, March 24 (AP)—An 18-year-old college honor student died yesterday of an injection of bacterially contaminated blood given during an experiment connected with war research on blood preservation by the University of Washington.

James Stanley Leedom, a freshman at Seattle University, was one of forty volunteers who participated in the project seeking better ways to preserve whole blood.

He died three days after the injection despite every effort to save his life.

Dr. Robert H. Williams, head of the University of Washington Department of Medicine, said the blood had become contaminated "by some phenomenon" after it had been refrigerated.

"The only way we can explain it," said Dr. Williams, "is that the bacteria was able to grow in some manner while the blood was at freezing temperature and not at body temperature."

Both Dr. Williams and Dr. Clement A. Finch, Associate Professor of Medicine in charge of hematology at the university, said they would "gladly participate in the same experiment tomorrow."

They said the bacteria had not yet been identified, but they believed it to be a saprophyte (any organism living on dead or decaying organic matter) that does not grow at body temperature but



Associated Press Wirephoto

James Stanley Leedom

thrives when chilled. It produces shock and high fever.

The father, Stanley P. Leedom, said he held no one at fault for his son's death.

"I don't blame anyone for this," he said. "I just don't want this tragedy to deter in any way from the blood donor program or these experiments."

The boy had planned to major in medicine.

Polio Epidemics



*Your dimes
did this
for me!*

**JOIN the
MARCH
of DIMES**
JANUARY 14-31

THE NATIONAL FOUNDATION FOR INFANTILE PARALYSIS, INC.
FRANKLIN D. ROOSEVELT, FOUNDER

Polio epidemic c. 1952





PARENTAL REQUEST FOR PARTICIPATION OF CHILD IN POLIOMYELITIS VACCINATION FIELD TRIAL

The National Foundation for Infantile Paralysis, Inc., in cooperation with state and local health, medical and educational authorities, is conducting a nation-wide field study of the effectiveness of a vaccine which may be protective against paralysis due to poliomyelitis. The vaccine consists of chemically killed poliomyelitis virus of all three known types. For purposes of this study, several thousand children will be given three injections of this vaccine into the arm over a period of several weeks; at least an equal number of unvaccinated children will be observed so that a comparison can be made between the two groups. The children in each group, those who are vaccinated and those who are not, are equally important to the study. In certain instances it will be necessary to test small samples of blood at intervals during the study to determine the amount of antibodies against poliomyelitis that are present.

I HEREBY REQUEST that my child, _____, be vaccinated
(first name) (middle name) (last name)
if selected, or otherwise be permitted to participate in the procedures described above without cost to me.

Date _____

Signed _____

Relationship to Child _____
(Must be parent or legal guardian)

School _____

(Street Address or Rural Location)

Grade _____

(City, Town or Township)

(State)

By the 1960s no longer faith in medical researchers

Revelation of
apparent
abuses of
human
subjects,
especially the
Tuskegee
Syphilis Study

Henry
Beecher's
bombshell

HENRY K. BEECHER, M.D.



Professor of
Anesthesia Research
at Harvard Medical
School

Convener of the
Harvard Ad Hoc Brain
Death Committee

“Ethics and Clinical Research”

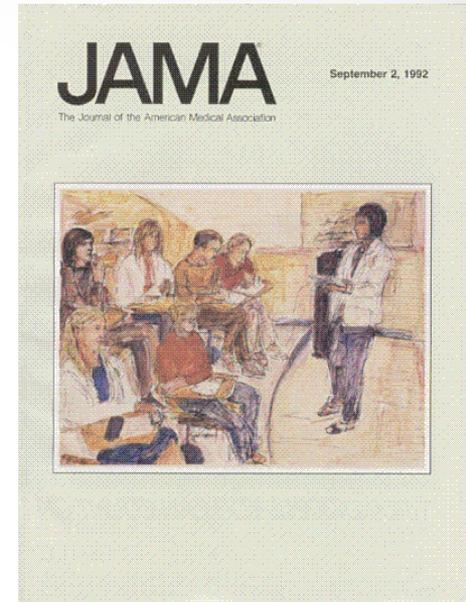
*New England Journal of
Medicine* 1966

22 examples of “questionable” research practices

Not from fringe BUT from mainstream
researchers and institutions



5



2



5



2

Cover picture: Localization of tropomyosin (green) and α -actinin (red) in cardiomyocytes isolated from a nontransgenic control (left) and tropomyosin overexpressing transgenic (TGT) mouse (right). Control cells show little or no overlap (yellow) between tropomyosin and α -actinin foci in control cells, but the abundant yellow signal in TGT cells indicates abundant colocalization of tropomyosin with α -actinin. See the article by Sessman et al., pp. 51-61.

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Publication of the 22 examples

the rest from

*Science, Cancer, J. of
Urology, Surgery,
Gynecology and Obstetrics,
American J. of Medicine,
Anesthesiology, and
American J. Med. Sciences*

Why HENRY K. BEECHER?



Christian faith?

anesthesia?

experience with
human subjects
research?

Nazi Experiments



1946-47, prosecution of 23 Nazi medical personnel



United States v. Karl Brandt et al



Permissible Medical Experiments

The Nuremberg Code



First principle

.The voluntary consent of the human subject is absolutely essential.

Strictly interpreted, the first principle would eliminate experiments on children, prisoners, the dying, the mentally ill

efforts to create a more workable code

The Declaration of Helsinki (1964)

Beecher concerned about
new researchers who fail to
understand their
responsibilities

Who were the research subjects in Beecher's 22 examples?

“mentally defective” children
mentally retarded and delinquent children
the very elderly
soldiers in the armed forces
charity patients
terminally ill
alcoholics
children and newborns
patients at the NIH Clinical Center

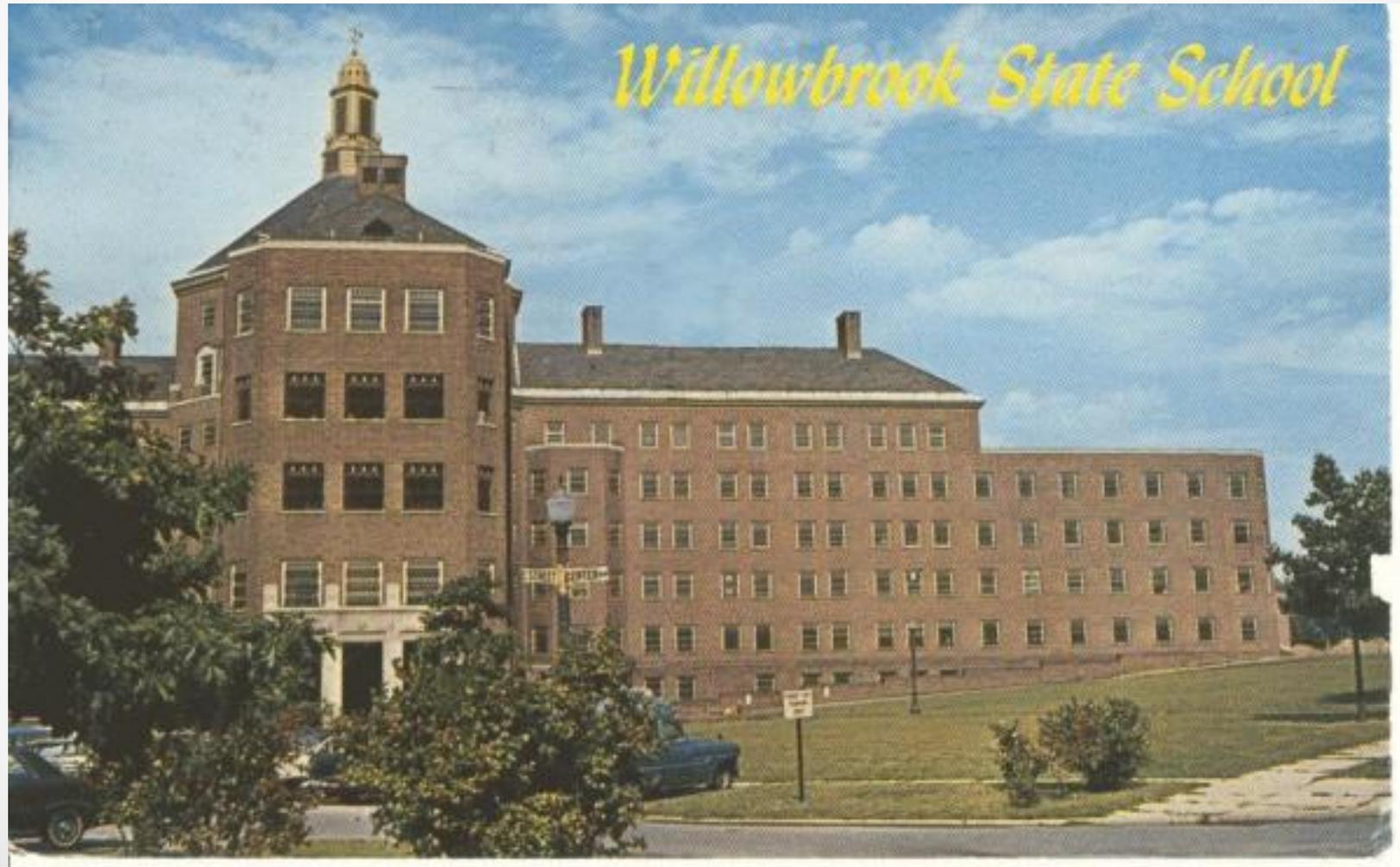
Example 4

Study of effects of new antibiotic for treating acne using juvenile delinquents

the drug associated with liver problems

teenagers undergo repeated liver biopsies

Example 16





Dr. Saul Krugman et al
begin studies to
acquire information
about the natural
history of hepatitis and
work toward vaccine

Willowbrook studies

Newly admitted children (whose parents give consent) are given intramuscular injections of hepatitis or “milkshakes” with hepatitis



Krugman continued to defend the studies but issues persisted about informed consent, coercion, and study design (withholding gamma globulin)



SAUL KRUGMAN, M.D.

Example 17

Jewish Chronic Disease Hospital case

Funded by USPHS and American
Cancer Society

Injections of live cancer cells into
elderly patients without
consent

"did not wish to stir up any
unnecessary anxieties in the
patients" who had "phobia and
ignorance" about cancer.

The New York Times

Syphilis Victims in U.S. Study Went Untreated for 40 Years

By JEAN HELLER
The Associated Press

WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings with syphilis, who were induced to serve as guinea pigs, have gone without medical treatment for the disease and a few have died of its late effects, even though an effective therapy was eventually discovered.

The study was conducted to determine from autopsies what the disease does to the human body.

Officials of the health service who initiated the experiment have long since retired. Current officials, who say they

have serious doubts about the morality of the study, also say that it is too late to treat the syphilis in any surviving participants.

Doctors in the service say they are now rendering whatever other medical services they can give to the survivors while the study of the disease's effects continues.

Dr. Merlin K. DuVal, Assistant Secretary of Health, Education and Welfare for Health and Scientific Affairs, expressed shock on learning of the study. He said that he was making an immediate investigation.

The experiment, called the Tuskegee Study, began in 1932 with about 600 black men,

July 25, 1972



Study begins in 1932



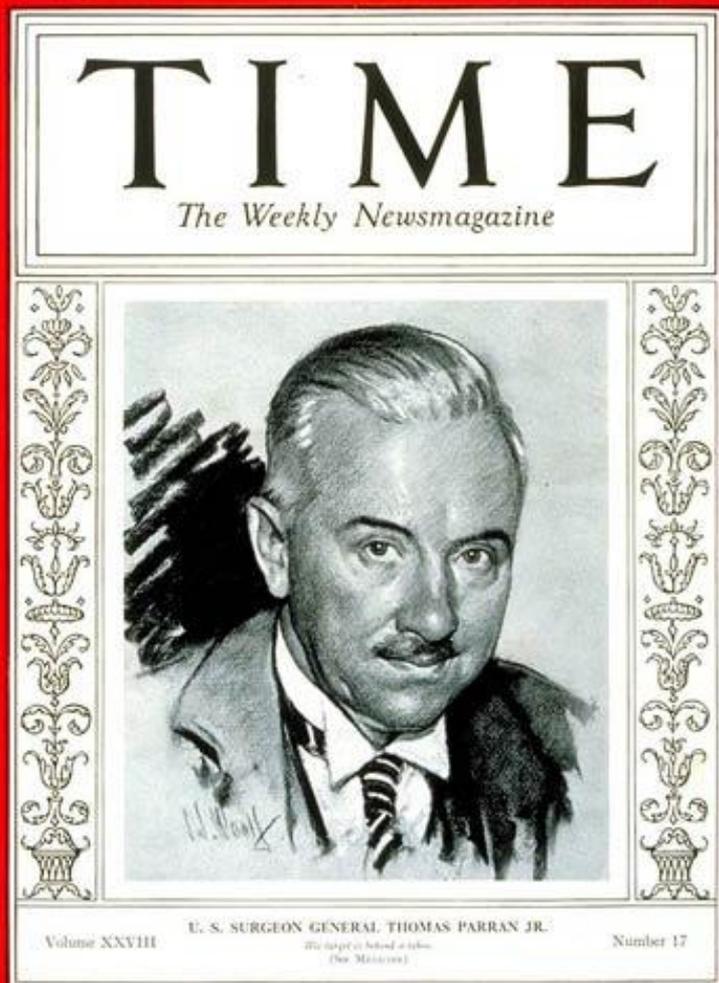
(Courtesy National Archives)



PHS Surgeon General Thomas Parran,

*Shadow on the
Land*

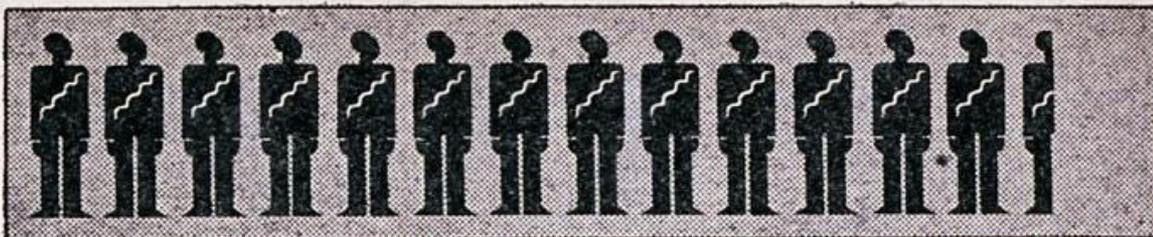
Head of PHS, 1936-
1948



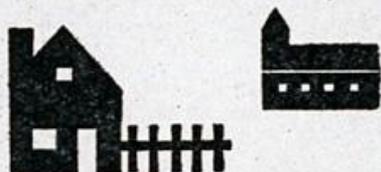
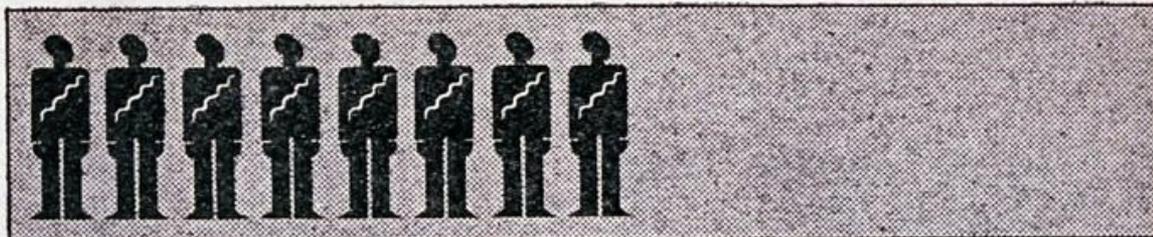
INCIDENCE OF SYPHILIS AMONG NEGROES



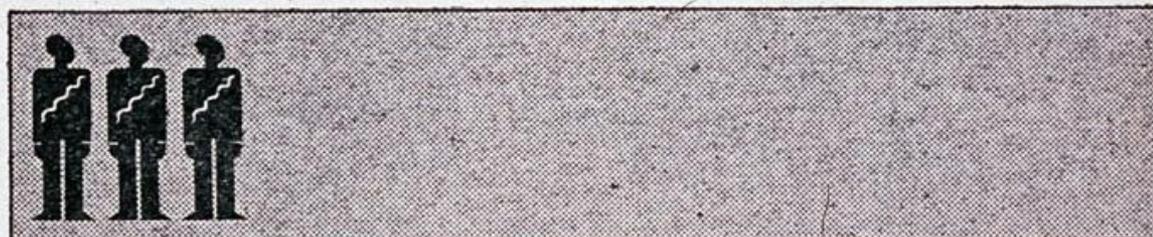
MACON COUNTY, ALA.



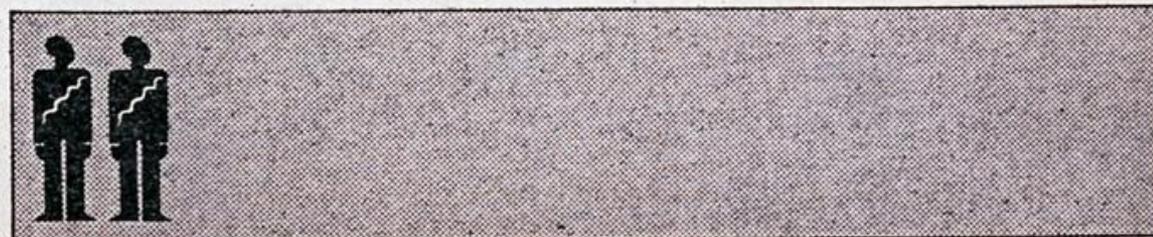
BOLIVAR COUNTY, MISS.



ALBEMARLE COUNTY, VA.



MEHARRY UNIVERSITY, TENN.



Each symbol represents 3% of all Negroes studied

PICTORIAL STATISTICS, INC 

From treatment to “a study in nature”



Dr. Raymond Vonderlehr offers Negro men “last chance for special free treatment” for their “bad blood”

Lumbar puncture (to obtain spinal fluid for diagnosis)







World War II

- PHS asks Tuskegee draft board to exempt the men in the study from the draft
- They serve in another war

Nurse Eunice Rivers



Nurse Rivers

obtains permission
for autopsy

easier when a
burial stipend of
\$50 is provided

only one refusal in
140 requests

Figure 3. An unaltered view. Nurse Eunice Rivers measures a participant in the TSUS. Dr. Stanley Schuman records the data. The photograph was taken in the TVAH in February 1952. (National Archives, CDC, East Point, GA)

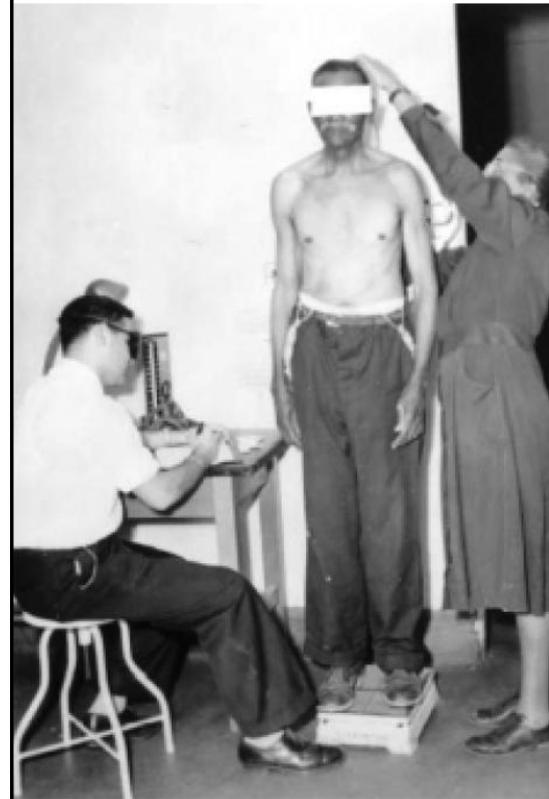


TABLE I. TABULAR LISTING OF DIFFERENCES IN THE UNTREATED SYPHILIS STUDIES IN ALABAMA AND IN NORWAY

	ALABAMA	NORWAY
Study population composition	Rural Negro men	White men and women
Control	Nonsyphilitic controls observed	No controls
Percentage autopsied of those who have died	63.3 per cent	24.3 per cent
Patient motivation for study participation	Volunteers with social incentives	Sickness and disability
Treatment status	Small amounts, especially in younger men	Less treatment available, especially in early years of study
Clinical facilities	Newer x-ray, EKG, and serologic techniques	Best medical facilities of the time (1925-1927)
Spinal fluid examination	Most of the syphilitic patients had spinal fluid examinations at start of study	No routine spinal fluid examination reported
Selection of patient material	Acute syphilis and younger patients treated and omitted at start of study; early and late latent patients studied and followed	Only early, untreated syphilis included

1954

” for the first time, men in the study identified as “volunteers with social incentives”

U. S. PUBLIC HEALTH SERVICE

25

This certificate is awarded to

In grateful recognition of 25 years
of active participation in the
Tuskegee medical research study.

Awarded 1958



Leroy C. Burney

Surgeon General

1969

CDC convenes a blue-ribbon panel to determine whether Tuskegee study should continue

only physician not familiar with the Study argues that the experiment should end and the men receive treatment

the Study continues until 1972

Study Revealed July 25, 1972





- Kennedy holds hearings on human experimentation including the TSS
- Legislation passed 1974
- National Research Act

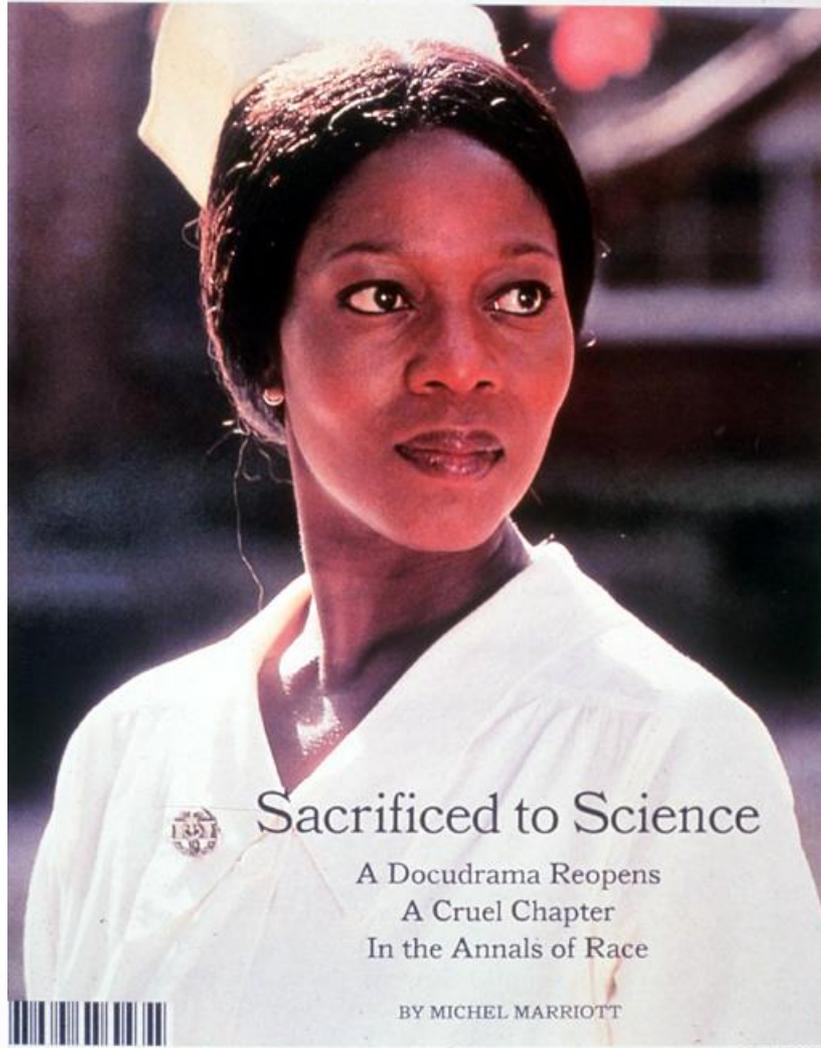
1974 National Research Act

creation of a National Commission to study the moral issues posed by human experimentation

new federal regulations for IRBs and written informed consent

Television

FEBRUARY 16-22



Sacrificed to Science

A Docudrama Reopens
A Cruel Chapter
In the Annals of Race

BY MICHEL MARRIOTT



Persistent stories about the deliberate infection of the men in Tuskegee with syphilis

The AIDS 'Plot' Against Blacks

Bizarre as it may seem to most people, many black Americans believe that AIDS and the health measures used against it are part of a conspiracy to wipe out the black race.

A survey of black church members in 1990 found that an astonishing 35 percent believed AIDS was a form of genocide. A New York Times/WCBS-TV News poll in 1990 found that 1 black in 10 believes the AIDS virus was "deliberately created in a laboratory in order to infect black people" and an additional 2 in 10 thought that might be so. A Gallup/Newsweek poll in March produced similar results.

Even some dedicated black health workers engaged in the fight against AIDS decline to disavow these fears. Testifying before the National Commission on AIDS, one said that "until proven otherwise" she considered AIDS a man-made disease.

Worse yet, the treatments and preventives against AIDS have become suspect. Some blacks believe that AZT, the harsh drug used to combat the disease, is a plot to poison them

... that campaigns urging use of condoms, the best way to prevent sexual transmission, are a scheme to reduce the number of black babies ... that distributing clean needles to slow transmission among addicts is a plot to encourage drug abuse.

At its most destructive, the paranoia causes many blacks to avoid medical treatment. Unless black and Hispanic leaders play a more vigorous role in countering the fears and mistrust, it will become ever harder to slow the epidemic.

The task is urgent because the disease is now spreading most rapidly among minorities. Last year, for the first time, the number of AIDS cases reported for minorities exceeded the number for whites. Most worrisome for the future, blacks account for a majority of AIDS cases in women and children. "AIDS in future generations may be primarily a disease of black people," the New York Department of Health warned last month.

Yet the response to this growing crisis has been sluggish. Financially pressed minority organizations and local governments have little energy for fighting AIDS, especially given the stigma attached to its main victims, homosexuals and drug addicts. But whether financing for minority AIDS programs has lagged behind white programs, as some black leaders charge, is not clear. Federal and state funds to minority AIDS organizations have gone up and the Government's central programs, like counseling and testing services, have huge minority caseloads.

No programs, even if well financed, will succeed without a change in attitudes. Thus it is welcome news that the New York State Health Department, with the help of black politicians and community leaders, has started a media campaign to encourage blacks to mobilize against AIDS.

The campaign rightly stresses that AZT and condoms are not plots against blacks. But it refuses to counteract the paranoia about AIDS as genocide, saying only that no matter

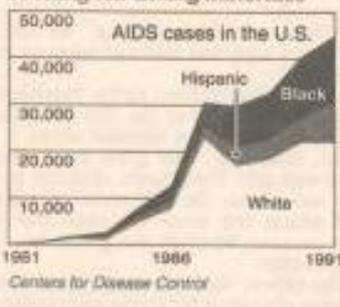
how AIDS got started, there are ways to stop it. Campaign officials reasoned that few blacks would believe government denials anyway. But surely black leaders and public figures with high credibility, such as Magic Johnson, the basketball star, could do much to discredit the pernicious and dispiriting rumors.

Meanwhile, Federal, state and local health officials need a far better assessment of the flow of AIDS money into minority communities and stronger programs to fight the disease there. Costly drug treatment ought to be provided to all who seek it, an investment that would yield dividends far beyond slowing the spread of AIDS. And more vigorous outreach programs might persuade more individuals to avoid risky behavior.

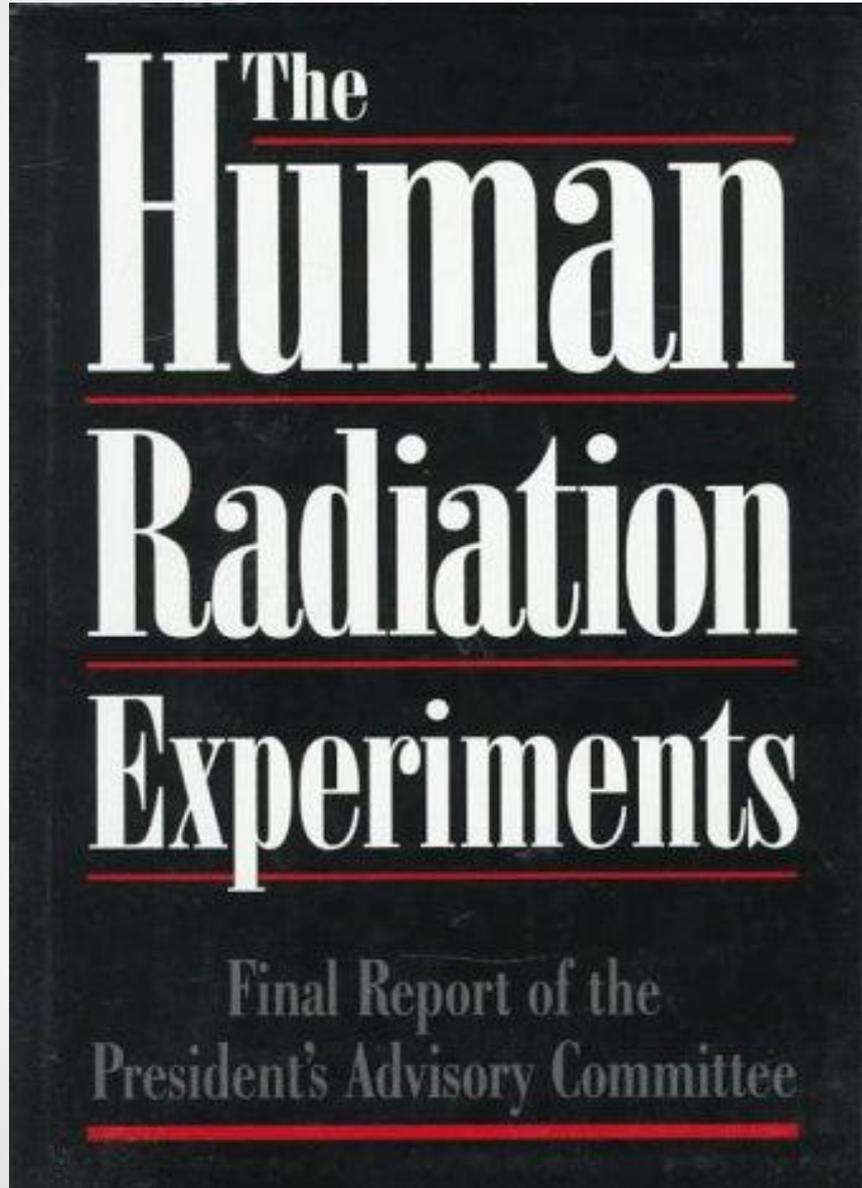
As white Americans, shaken by the riots in Los Angeles, search for ways to help afflicted and distrustful minorities, there's no wiser way to start than AIDS. A failure to treat and prevent AIDS among minorities: That would be the true genocide.

The Plague Spreads

A rising toll among minorities



Presidential apology 1995



White House Apology for the Syphilis Study, May, 1997





White House apology ceremony, 16 May 1997. Participants and survivors of the study (first row): Herman Shaw, Fred Simmons, Charles Pollard, Frederick Moss, Carter Howard. White House officials (back row): U.S. Surgeon General David Satcher, President William J. Clinton, Vice-President Albert Gore.

Wielding the “Tuskegee Analogy”

In 1997 *NEJM* acting editor Marcia Angell compares placebo-controlled trials for preventing vertical transmission of HIV from mothers to infants to the Tuskegee Study

2001

Maryland State Supreme Court rules that families can sue the Kennedy-Krieger Institute (JKHMI), comparing the research on effects of lead paint on children to both Nazi experiments and the Tuskegee Study.

President Bush vetoes stem cell research bill, summer 2006

research on human stem cells
“constitutes a grave violation of human rights just as we saw in the Tuskegee experiments here in the United States and in the Nazi experiments of World War II.”



Scandal, tragedy
and revelation
continues

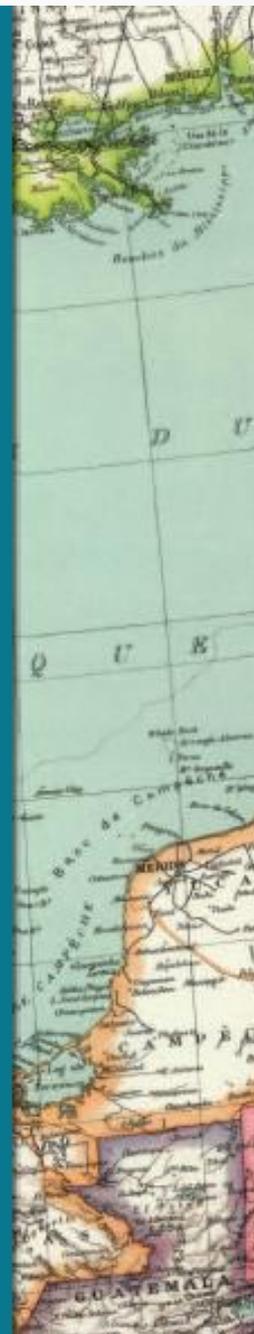
2011



“ETHICALLY IMPOSSIBLE”
STD Research in Guatemala
from 1946 to 1948

Presidential Commission
for the Study of Bioethical Issues

September 2011



John Cutler

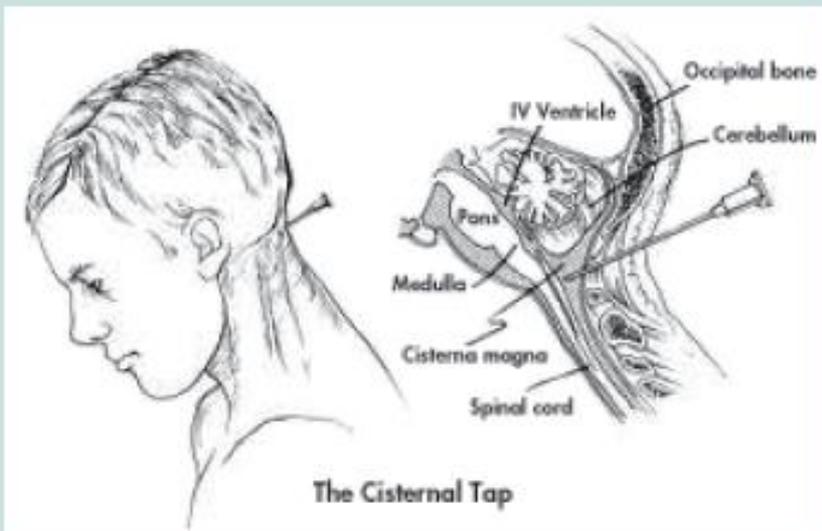


Diagram of a cisternal puncture.
From Alexander G. Reeves, M.D. and Rand S. Swenson,
M.D., Ph.D., "Disorders of the Nervous System"



John C. Cutler
From the National Library of Medicine

“I saw Doctor Parran on Friday [February 14] and he wanted to know if I had had a chance to visit your project. Since the answer was yes, he asked me to tell him about it and I did so to the best of my ability. He was familiar with all the arrangements and wanted to be brought up to date on what progress had been made. As you well know, he is very much interested in the project and a merry twinkle came into his eye when he said, ‘You know, we couldn’t do such an experiment in this country.’”⁵⁸¹

Learning the past,
living with the past,
forming the future